PROCESSING PHEROMONES

The mouse vomeronasal organ (VNO) is a tubular structure located in the nasal cavity just above the roof of the mouth. Chemical signals enter the VNO through an opening at the base of the nasal cavity 1, where they enter the organ’s lumen. Projecting into the lumen are sensory neurons outfitted with vomeronasal receptors (VRs), G protein-coupled receptors that initiate intracellular signaling cascades when bound by a ligand, converting pheromone signals into electrical nerve pulses 2. Those signals are then sent to glomeruli in the accessory olfactory bulb (AOB), where they are relayed to mitral cells that project into deeper brain regions 3. In areas like the amygdala and the hypothalamic nuclei, that information is further processed and used to effect changes in the animal’s behavior and physiology 4.

The AOB connects directly to the amygdala and the hypothalamic nuclei, bypassing the cortex, suggesting that pheromones can trigger endocrine changes and behavioral responses without conscious thought.

Each VNO neuron expresses a receptor from one of three main families: V1Rs, which are similar to odorant receptors in the nose; V2Rs, which may have evolved from the ancestral taste receptors; and formyl peptide receptors (FPFRs), innate immune receptors that were recently discovered to serve as chemosensory receptors in the mouse VNO. When a pheromone binds its receptor, it activates a G-protein bound to the inside of the cell membrane A, triggering a cascade of intracellular signals that leads to the activation of multiple ion channels, including TRPC2 B.

The molecules that trigger the VRs are still largely unknown in mammals. Putative pheromones include: small molecules, major urinary proteins (MUPs), and major histocompatibility complex (MHC) peptides.

Deletion of G12, the main G protein for VNO neurons expressing the V1Rs, causes a decrease in copulation and intermale aggression. Deletion of G12, the main G protein for VNO neurons expressing the V2Rs, leads to the loss of aggression in both male and female mice.

Mice lacking the TRPC2 ion channel exhibit neither territorial aggression nor maternal aggression.

VNO neurons expressing the same VRs project to multiple glomeruli in stereotopic patterns, helping the animals discern between different chemical signals.